UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/940,682	08/27/2001	David E. Townsend	150026.464	4343

500 7590 09/06/2007

SEED INTELLECTUAL PROPERTY LAW GROUP PLLC
701 FIFTH AVE
SUITE 5400
SEATTLE, WA 98104

EXAMINER	
FORD, ALLISON M	
ART UNIT	PAPER NUMBER
1651	

MAIL DATE	DELIVERY MODE
09/06/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/940,682	TOWNSEND, DAVID E.	
	Examiner	Art Unit	
	Allison M. Ford	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5,7,10-13,15,16,25 and 26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5,7,10-13,15,16,25 and 26* is/are rejected.

7)☒ Claim(s) *1,5,7,10-13,15,16,25 and 26* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants response of 15 June 2007 have been received and entered into the application file. Claims 1, 5, 13, 15, 16 and 25 have been amended; claims 2-4, 6, 8, 9, 14 and 17-24 are cancelled; claims 1, 5, 7, 10-13, 15, 16, 25 and 26 remain pending in the current application, all of which have been considered on the merits.

Priority

Acknowledgement is made of applicant's claim for priority to provisional application 60/228,956, filed 28 August 2000, priority under 119(e). This provisional application provides support for all claims; thus all claims are given the effective filing date of 28 August 2000.

Applicant's claim for the benefit as a CIP of prior-filed application US 08/484,593 (now US Patent 6,387,650) under 35 U.S.C. 120 is also acknowledged. However, this prior filed application does not provide support for the subject matter of current claim 7, which requires the conditionally detectable marker to comprise tetrazolium red. Therefore, only claims 1, 5, 10-16, 25 and 26 receive the benefit of the effective filing date of 7 June 1995.

Response to Arguments/Amendments

Applicant's remarks and amendments to the claims, filed 15 June 2007, have been fully considered.

The amendments have obviated the rejection(s) under 35 USC 112, second paragraph.

With regards to the rejection(s) under 35 USC 103(a), Applicant has incorporated the limitation of claim 14 (indicated as free of art) into the independent claims. Additionally, Applicant has argued that the present invention fulfills a long felt need; Applicant points out that the cited references are from 1990

and 1991, which they feel is indicative to support that such a composition as currently claimed has not been produced during the interim.

In response, it is first submitted that the allowability of the limitation of previous claim 14 (now incorporated into claims 1 and 25) is regrettably withdrawn upon reconsideration of the present claim set. The following rejections are newly applied and constitute the complete set of rejections applied to the instant claims. However, in response to Applicant's argument that the current invention fulfills a long felt need, Applicant has not established a showing of long felt need, nor that the current invention was the first to satisfy any such need. Establishing long-felt need requires objective evidence that an art recognized problem existed in the art for a long period of time without solution. The relevance of long-felt need, and the failure of others, to the issue of obviousness depends on several factors. First, the need must have been a persistent one that was recognized by those of ordinary skill in the art. *In re Gershon*, 372 F.2d 535, 539, 152 USPQ 602, 605 (CCPA 1967). Second, the long felt need must not have been satisfied by another before the invention by Applicant. *Newell Companies v. Kenney Mfg. Co.*, 865 F.2d 757, 768, 9 USPQ2d 1417, 1426 (Fed. Cir. 1988). Third, the invention must in fact satisfy the long felt need. *In re Cavanagh*, 436 F.2d 491, 168 USPQ 466 (CCPA 1971). It is respectfully submitted that Applicant's argument as to the date of the cited references are not impressive absent a showing that the art tried and failed to solve the same problem notwithstanding its presumed knowledge of the references. See *In re Wright*, 569 F.2d 1124, 193 USPQ 332 (CCPA 1977). Applicant has failed to establish a long felt need which has not been satisfied until their application. Thus these arguments are not found persuasive.

Claim Objections

It is noted that the amended claims have a number of formatting errors, specifically the spacing between words within the body of the claims is askew. For example, in claim 1, line 3 "an

aminopeptidase,wherein said..." It appears the majority of the errors are a result of using the "justify" alignment tool; it is requested Applicants use the "align left" setting.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 5, 7, 13, 15, 16 and 25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant's claims are directed to a composition for detecting a target microorganism, comprising (i) a growth-supporting medium for the target microorganism; (ii) a conditionally detectable marker that undergoes a color change when reacted upon by a viable microorganism (a viability marker); and (iii) an aminopeptidase substrate comprising a signal moiety capable of providing a detectable signal when cleaved, wherein the aminopeptidase which would react upon the substrate is not produced by the target microorganism. Claim 1 and dependents thereof define the target microorganism as one of *Salmonella, Listeria, E. coli* OH157, *Campylobacter, Staphylococcus aereus, Cryptosporidium*, and *Giardia*. Claim 25 requires the target microorganism to be *Campylobacter.*

The claims are found to lack written description for the aminopeptidase substrate, as claimed.

To satisfy the written description requirement, the specification must provide sufficient description of the claimed product (in the instant case, the composition comprising the aminopeptidase substrate, as defined by the claims) to show that Applicant was in possession of the claimed invention.

It is noted the specification does provide numerous aminopeptidase substrates and even numerous L-alanine aminopeptidases, the disclosed species are representative of aminopeptidase substrates, in general, and of L-alanine aminopeptidase substrates; however, the claimed composition does not include "aminopeptidase substrates," in general, or even "L-alanine aminopeptidase substrates," but aminopeptidase substrates *wherein the aminopeptidase is substantially absent from at least one of the listed target microbes*. Therefore, the invention as claimed is directed to a narrower subgenus of aminopeptidase substrates than disclosed in the specification. Even though Applicants have described a *broader* genus than that which they are claiming, the problem of a lack of written description is still present because Applicant's disclosure fails to define or describe a representative number of species which would show Applicant was in possession of the *narrower* subgenus of substrates being claimed. When the scope of the claims is narrower than what is disclosed in the specification, there must be support and description for that specific subgenus, by itself, not just as falling within the broader genus. It has been held that disclosure of a "laundry list" of species does not constitute a written description of every species in the genus, much less a subgenus, because it would not "reasonably lead" those skilled in the art to any particular species, See *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1571, 39 USPQ2d 1895, 1905 (Fed. Cir. 1996).

It must be shown that Applicant had possession of the invention *as claimed* (i.e. the narrowed subgenus of aminopeptidase substrates which satisfy the claim limitations), and must describe it in a way that would permit one of ordinary skill in the art to immediately envisage the claimed invention (e.g. the narrowed subgenus). Because Applicant has not disclosed specific aminopeptidases that are absent from *each* of the claimed target microbes, one could not immediately envisage which aminopeptidase substrates would appropriately be included in the claimed composition.

Claims 1, 5, 7, 10-13, 15, 16 and 25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for production and use of compositions for identifying a pure culture sample of Gram-negative bacteria as *Campylobacter*, said compositions comprising (i) a conditionally detectable marker that functions as a viability marker; (ii) an L-alanine aminopeptidase substrate; and (iii) a growth-supporting medium for *Campylobacter*, does not reasonably provide enablement for production and use of compositions for detecting any target microorganism in any sample, or even for detecting *Campylobacter* in a mixed sample, or for differentiating between *Campylobacter* and any Gram-positive bacteria, wherein said composition comprises (i) a conditionally detectable marker that functions as a viability marker; (ii) a substrate for an aminopeptidase, wherein said aminopeptidase is substantially absent from the target microorganism; and (iii) a growth-supporting medium for *Campylobacter*. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Analysis of whether a particular claim is supported by the disclosure in an application requires a determination of whether that disclosure, when filed, contained sufficient information regarding the subject matter of the claims as to enable one skilled in the pertinent art to make and use the claimed invention without undue or unreasonable experimentation. See *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916). The key word is 'undue,' not experimentation.' " (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Applicant's claims are directed to a composition for detecting a target microorganism, wherein the composition comprises (i) a conditionally detectable marker that undergoes a color change when reacted upon by a viable microorganism (a 'presumptive indicator'); (ii) an aminopeptidase substrate comprising a signal moiety capable of providing a detectable signal when cleaved, wherein the aminopeptidase which would react upon the substrate is substantially absent from the target

microorganism, but is present in non-target microorganisms (a 'confirmation indicator') (See Spec. pg. 17); and (iii) a growth-supporting medium for *Campylobacter*. A target microorganism is detected when a sample, placed in contact with the claimed composition, produces a positive signal by the 'presumptive indicator,' but fails to produce a positive signal by the 'confirmation indicator'; if non-target microorganisms are present, two positive signals would be produced. Though the claims are not directed to a method of using the claimed composition, it is necessary to set forth how the claimed composition would be used, so as to determine whether the disclosure enables one of ordinary skill in the art to successfully make and use the claimed composition.

Therefore, in order to successfully make and use the claimed composition, one of ordinary skill in the art would have to be able to determine (a) a conditionally detectable marker that would undergo a color change when reacted upon by any viable microorganism; and (b) an aminopeptidase substrate comprising a signal moiety that would produce a detectable signal when cleaved by the appropriate aminopeptidase, wherein the aminopeptidase is substantially absent from the target microorganism, but would be present in all non-target microorganisms. A review of the specification shows that sufficient number of viability markers were disclosed in the specification (e.g. Vital Dyes, specifically tetrazolium red), or were otherwise known in the art, to enable the artisan of ordinary skill to be able to select an appropriate viability marker for use in the composition. However, with regards to the aminopeptidase substrate which would satisfy the claim limitations, the specification fails to disclose a representative number of aminopeptidase substrate species which would be suitable for use in the claimed invention, for each of the claimed target microorganisms.

As discussed above, though Applicant has disclosed numerous aminopeptidase substrates, they have not identified which substrates, from the lengthy lists provided, would be suitable for use in the claimed composition for detection of each of the claimed target microorganisms. Within claim 1, the target microorganism are defined as one of *Salmonella, Listeria, E. coli* OH157, *Campylobacter,*

Staphylococcus aereus, Cryptosporidium, and *Giardia*; claim 25 is limited to *Campylobacter*. The specification only discloses that *Campylobacter* lacks L-alanine aminopeptidase (See Spec, page 18); there are no teachings or discussion of additional aminopeptidases which are substantially absent from *Campylobacter*, or of *any* aminopeptidases which are substantially absent from each of *Salmonella, Listeria, E. coli* OH157, *Staphylococcus aereus, Cryptosporidium*, and *Giardia*. Therefore, beyond the use of L-alanine aminopeptidase substrate for detection of *Campylobacter*, in order to successfully make and use the claimed composition, one of ordinary skill in the art would first have to conduct experimentation to determine which, if any, aminopeptidases are substantially absent from each of the claimed target microorganisms and which *is* present in all non-target microorganisms; such is considered to amount to undue experimentation. While it would not be outside the purview of the artisan of ordinary skill to test various microorganisms for different aminopeptidases, due to the large number of aminopeptidases known (which would each need to be tested), and the almost infinite number of microorganisms (again, which would each need to be tested in order to ensure the target microorganism is the only one that substantially lacks the aminopeptidase in question), the amount of experimentation which would be required on the part of the artisan would be considerably extensive and undue. The disclosure does not even present a narrowed range of probable or likely aminopeptidases which could be reasonably expected to be present in all but the target microorganism.

The only embodiment Applicant has clearly enabled is for when the composition is intended for identification of a pure culture sample as *Campylobacter*, wherein the composition comprises (i) a conditionally detectable marker that functions as a viability marker (e.g. tetrazolium red); (ii) an L-alanine aminopeptidase substrate; and (iii) a growth substrate for *Campylobacter*. However, even though Applicant has disclosed how to make this particular composition, it is noted that such a composition would only be able to successfully identify a pure culture sample as *Campylobacter* if it was known previously that the culture was Gram-negative. It was known most Gram-negative bacteria contain the L-

alanine aminopeptidase in their cell wall; *Campylobacter* spp are the only Gram-negative bacteria that are negative for L-alanine aminopeptidase. All Gram-positive bacteria are negative for L-alanine aminopeptidase (See, e.g. Manafi et al). Therefore, the composition in question would only be able to identify a L-alanine aminopeptidase negative sample if the sample was free of L-alanine aminopeptidase positive microorganisms; the presence of any L-alanine aminopeptidase containing bacteria in the sample will prevent the identification (detection) of *Campylobacter*. Both *Campylobacter* and all Gram-positive bacteria samples will give the same reading (positive 'presumptive indicator'/negative 'confirmation indicator'); therefore it would be necessary to know the same being applied is not Gram-positive, but Gram-negative.

Beyond this scope, Applicant has not enabled one skilled in the pertinent art to make and use the claimed invention without undue or unreasonable experimentation.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 5, 7, 10-16 and 25-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Manafi et al (J Appl Bacteriol, 1990) in view of Molina et al (Enfermedades Infecciosas y Microbiologia Clinica, 1991) and Tuompo et al (US Patent 5,420,017).

Applicant claims 1 and 25 are directed to a composition for detecting a target microorganism, specifically *Campylobacter*, in a sample, the composition comprising (i) a conditionally detectable marker that undergoes a color change when reacted upon by a viable microorganism; (ii) a substrate for an aminopeptidase, wherein said substrate comprises a signal moiety that provides a detectable signal when

cleaved; and (iii) a growth supporting medium for the target microorganism; and wherein the (i) conditionally detectable marker and (ii) the substrate for an aminopeptidase are not the same molecule. Claim 7 requires the conditionally detectable marker to be tetrazolium red. Claims 10 and 26 require the aminopeptidase to y be L-alanine aminopeptidase. Claims 11 and 12 require the substrate to be selected from the disclosed group, specifically L-alanin-7-amido-4-methylcoumarin.

Claims 5 and 13 are directed to the intended use of the composition (detection of specific microorganisms), these claims recite specific target microorganisms as well as the non-target microorganisms the composition is to detect.

With regards to claims 5 and 13, which are related to the intended use of the composition (detection of specific microorganisms), please note that in cases where the body of the claim fully and intrinsically sets forth all the limitations of the invention, such as all components of a composition, recitations that merely states the intended use of the composition, rather than any distinct definition of any of the claimed invention's limitations, are not considered limitations and are of no significance to claim construction. See MPEP § 2111.02. Therefore, claims 5 and 13 are given no patentable weight and have been included in the rejection of the claims directed to the composition.

Manafi et al disclose a method and composition for detecting the presence of Gram-negative bacteria in a sample. The composition of Manafi et al comprises the conditionally detectable marker L-alanine-7-amido-4-methylcoumarin (AAMC), which produces a fluorescent color change when cleaved by the L-alanine-aminopeptidase found in the cell wall of substantially all Gram-negative bacteria except for *Campylobacter* (See Manafi et al, See pages 823, first paragraph & Molina et al, abstract). Manafi et al disclose the fluorogenic substrates were incorporated into Plate Count Agars (which necessarily contain the necessary nutrients and growth factors necessary for the survival of the plated microorganisms, as the bacterial cultures successfully grew on the agars) (See Manafi et al, Pg. 823, col. 2, "Media and Chemicals"). The method of Manafi et al is capable of differentiating between Gram-negative and Gram-

positive bacteria as a positive result (fluorescent indicator) is only achieved when Gram-negative bacteria having the L-alanine aminopeptidase are present in the sample.

Tuompo et al also disclose a method and kit for detecting microorganisms in a sample. The method relies on use of a composition comprising a chromogenic reagent in an amount effective to detect bacteria; preferably the chromogenic reagent is a tetrazolium salt, particularly triphenyltetrazolium chloride (tetrazolium red), which produces a color change from colorless to red upon biochemical reduction by viable bacteria (See Tuompo et al, col. 2, ln 25-35 & claim 4).

It would have been obvious to one of ordinary skill in the art, at the time the invention was made to modify the composition of Manafi et al, which comprised AAMC in an agar plate, to further include tetrazolium red, as taught by Tuompo et al. Including the viability marker tetrazolium red in the agar plate of Manafi et al, would provide an extra measure of quality control in the methods of Manafi et al, as the viability marker would provide a positive reading, indicating the bacteria were successfully transferred in a viable state to the agar plates. As disclosed, the composition of Manafi et al only provides a detectable signal if the sample contains L-alanine aminopeptidase, if the sample is L-alanine aminopeptidase negative, no signal is produced, yet there is no way to determine if the sample is merely negative for L-alanine aminopeptidase or if the sample was not successfully plated. Including the viability marker tetrazolium red would provide an extra measure to ensure the sample was transferred successfully and that a false negative was not obtained due to a dead sample.

Therefore, the invention as a whole would have been prima facie case obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Allison M. Ford whose telephone number is 571-272-2936. The examiner can normally be reached on 7:30-5 M-Th, alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Leon B Lankford, Jr
Primary Examiner
Art Unit 1651